Message

From: Detlef Knappe [knappe@ncsu.edu]
Sent: 4/9/2018 9:40:46 PM
To: McCord, James [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=McCord, James]
CC: Nadine Kotlarz [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=userc79d3fb6]; Strynar, Mark [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5a9910d5b38e471497bd875fd329a20a-Strynar, Mark]; Lindstrom, Andrew [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=04bf7cf26aa44ce29763fbc1c1b2338e-Lindstrom, Andrew]
Subject: Re: PFAS analysis in Blood

My impression was that we are still pretty far from a reporting limit of 0.1 ng/mL. If we can get there with high res, then we would not need a targeted option.
Detlef

On Mon, Apr 9, 2018 at 11:47 AM, McCord, James <mccord.james@epa.gov> wrote:

> It really depends on what your goal is for the study. Is there a targeted level you would like to be able to measure? The NHANES LLOD for the PFAS compounds they measure is 0.1ng/mL and I don't think we are too far off that goal as is. I would guess my current LoD is on the order of 100 fg on column and anything lower is starting to get into very non-standard MS tricks. I'm not sure the effort involved is worth the results if they aren't expected to be physiologically relevant concentrations.
>
> You do make an interesting point about multiple injection though. I'll need to check if I can hack the injection software to let me do that.
>
> --
>
> James McCord
>
> **From:** Detlef Knappe [mailto:knappe@ncsu.edu]
> **Sent:** Monday, April 9, 2018 11:03 AM
> **To:** McCord, James <mccord.james@epa.gov>
> **Cc:** Nadine Kotlarz <nkotlar@ncsu.edu>; Strynar, Mark <Strynar.Mark@epa.gov>; Lindstrom, Andrew <Lindstrom.Andrew@epa.gov>
> **Subject:** Re: PFAS analysis in Blood
>
> Thank you, James.
>
> Would it be worthwhile to do both targeted (MS1 or low res) Orbi PLUS non-targeted Orbi work? And could that be accomplished with a single injection or two injections in series?

But perhaps this won't be necessary if S/N ratio can be enhanced sufficiently through larger injection volume (and perhaps the Agilent cartridge).

Best,

Detlef

On Mon, Apr 9, 2018 at 8:44 AM, McCord, James <mccord.james@epa.gov> wrote:

Just to clarify my part. On Friday I did a good deal of optimization to try to increase the sensitivity of the MS side, as well as improve the chromatography. I was able to consistently observe all the spiked compounds except PFMOAA in the SRM+5 ng/mL spiked sample at levels ~ 10x above my instrumental noise. I can get an extra 2-5-fold increase in signal intensity using a targeted MS1 method on the Orbitrap, which is less desirable and can probably drop the sensitivity another order of magnitude if we use the low-res detector and/or single ion methods, which is even less desirable but a possibility. It really depends on the use case for the instrumental method. I still think having a higher injection volume gives us a lot more room to play with.

One small issue is that the peaks that we are observing for the PFAS compounds are well below what I have been using for the feature extraction threshold in our previous samples, so I am not sure how well NTA will find out of left field new things; we can certainly give it a shot though.

--

James McCord

From: Nadine Kotlarz [mailto:nkotlar@ncsu.edu]
Sent: Monday, April 9, 2018 8:05 AM
To: Strynar, Mark <Strynar.Mark@epa.gov>
Cc: McCord, James <mccord.james@epa.gov>; Detlef R. U. Knappe <knappe@ncsu.edu>; Lindstrom, Andrew <Lindstrom.Andrew@epa.gov>

Subject: Fwd: PFAS analysis in Blood

Good morning, Mark,

I can't come to EPA today but I will be there all day tomorrow. I wanted to share my notes with you in case you can move forward with the serum method development.

I grabbed some screen captures from the Orbitrap last week (see attached slides and comments below the slides). The major takeaways were:

1. 50 uL serum method + 25 uL injection volume gave best response for C8-C10, PFOS, and PFHxA in SRM 1957 but peak shape for C8-C10 compounds was only great in one of the triplicate preps

2. Response for nafion byproducts 1 and 2 looked good in terms of peak shape and proportional increase in signal from 1 ng/mL to 5 ng/mL spikes

3. We did not see 1 ng/mL or 5 ng/mL spikes of GenX or PFMOAA in SRM 1957 or calf serum

4. There is significant PFMOAA background

James said he was able to modify the method on Friday and did start to see GenX but he thinks purchasing a larger sample loop (up to 100 uL) will be helpful.

Some ideas for next steps:

1. test whether we can see 5 ng/mL GenX in methanol

2. prepare dilution series of GenX and PFMOAA and see where their response drops off
3. clean the source to reduce noise for PFMOAA
4. increasing the ratio of ACN:FA (acetonitrile was added at 10x the volume of formic acid used in the rodent serum method (Reiner et al., 2009))
5. increase the injection volume with increased sample loop size
6. consider the filters in the agilent paper Detlef shared (see attachment below) to improve signal/noise

Thanks,

Nadine

---------- Forwarded message ----------

From: **Detlef Knappe** <knappe@ncsu.edu>
Date: Thu, Apr 5, 2018 at 4:02 PM
Subject: Fwd: PFAS analysis in Blood
To: Nadine Kotlarz <nkotlar@ncsu.edu>, "Strynar, Mark" <Strynar.Mark@epa.gov>

Useful for serum method?

---------- Forwarded message ----------
From: <tarun.anumol@agilent.com>
Date: Thu, Apr 5, 2018 at 3:36 PM
Subject: PFAS analysis in Blood
To: knappe@ncsu.edu

Here is the application using EMR-L for reoval of lipids and protiens from Blood for analysis of PFAS.

Tarun Anumol, Ph.D.
Global Environment Market Manager
Segment Marketing
Agilent Technologies, Inc.

2850 Centerville Rd., Wilmington, DE 19808
T: +1 302 636 1517 | M: +1 302 419 8909 | www.agilent.com